The Millennium Cohort Study: Opportunities for PACT Act Research

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Overview

• Largest and longest running military cohort study
  – Initiated July 2001 (pre-9/11)
  – Planned to continue until 2068

• >260,000 military personnel enrolled between 2001–2021
  – All Service branches and components
  – Women and other underrepresented groups oversampled
  – 58% of participants have separated from service (2022)

• Research findings inform policy and programs
# Study Objective and Methodology

Determine the long-term health impacts of military service on Service members and Veterans; transition findings to improve and inform policy, interventions, and future research

<table>
<thead>
<tr>
<th>Enrollment panels:</th>
<th>Frequency:</th>
</tr>
</thead>
</table>

**Survey topics:** Mental and physical health, health behaviors, military exposures and other experiences (combat, deployment)

**Data integration:** Linkage with multiple enterprise military and medical databases
Multiple-Panel Design

Panel 1
- 2001-03: Wave 1
- 2004-06: Wave 2
- 2007-09: Wave 3
- 2011-13: Wave 4
- 2014-16: Wave 5
- 2019-21: Wave 6
- 2023-25: Wave 7

Panel 2
- 2001-03: Wave 1
- 2004-06: Wave 2
- 2007-09: Wave 3
- 2011-13: Wave 4
- 2014-16: Wave 5
- 2019-21: Wave 6

Panel 3
- 2001-03: Wave 1
- 2004-06: Wave 2
- 2007-09: Wave 3
- 2011-13: Wave 4
- 2014-16: Wave 5

Panel 4
- 2001-03: Wave 1
- 2004-06: Wave 2
- 2007-09: Wave 3
- 2011-13: Wave 4
- 2014-16: Wave 5

Panel 5
- 2001-03: Wave 1
- 2004-06: Wave 2
## Enrollment Panels

(N = 260,228)

<table>
<thead>
<tr>
<th>Panel</th>
<th>Enrollment Dates</th>
<th>Years of Service at Enrollment</th>
<th>Oversampled Groups</th>
<th>Roster Size (Date)</th>
<th>Total Contacted</th>
<th>Total Enrolled (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Jun 2004–Feb 2006</td>
<td>1–2</td>
<td>Women Marine Corps</td>
<td>150,000 (Oct 2003)</td>
<td>123,001</td>
<td>31,110 (25%)</td>
</tr>
<tr>
<td>3</td>
<td>Jun 2007–Dec 2008</td>
<td>1–3</td>
<td>Women Marine Corps</td>
<td>200,000 (Oct 2006)</td>
<td>154,270</td>
<td>43,438 (28%)</td>
</tr>
<tr>
<td>4</td>
<td>Apr 2011–Apr 2013</td>
<td>2–5</td>
<td>Women Married</td>
<td>250,000 (Oct 2010)</td>
<td>247,266</td>
<td>50,052 (20%)</td>
</tr>
<tr>
<td>5</td>
<td>Sep 2020–Jun 2021</td>
<td>1–5</td>
<td>Women Married</td>
<td>500,000 (Jun 2020)</td>
<td>444,285</td>
<td>58,609 (13%)</td>
</tr>
</tbody>
</table>

*Deployment to Southwest Asia, Bosnia, and/or Kosovo after August 1997.*
MCS Cohort Profile
Panels 1–5 (n ~ 260,228)

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>31</td>
</tr>
<tr>
<td>Racial or ethnic minority</td>
<td>31</td>
</tr>
<tr>
<td>Enlisted</td>
<td>82</td>
</tr>
<tr>
<td>Active component</td>
<td>70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current Status</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever deployed</td>
<td>60</td>
</tr>
<tr>
<td>Separated</td>
<td>58</td>
</tr>
<tr>
<td>Deceased</td>
<td>1.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean Current Age (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panel (Year)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1 (2001)</td>
</tr>
<tr>
<td>2 (2004)</td>
</tr>
<tr>
<td>3 (2007)</td>
</tr>
<tr>
<td>4 (2011)</td>
</tr>
<tr>
<td>5 (2020)</td>
</tr>
</tbody>
</table>

Note: Air Force proportion includes Space Force personnel.
# Research Portfolios

## Psychological Health
- Adverse Childhood Events
- Brain Health
- Community Impact on Families
- Economic and Occupational Outcomes
- Environmental Exposures
- Equity and Inclusion
- Family Retention
- Health Behaviors
- Illness and Injury

## Health-Related Behaviors
- Interpersonal Aggression
- Research Methodology
- Sexual Trauma
- Spouse Caregiving
- Substance Use
- Suicide
- Transitioning to Civilian Life
- Veteran Health
- Women’s Health

## Physical Health and Chronic Disease
Research Productivity

• ~150 peer-reviewed publications to date
  – Etiologic and hypothesis-driven analyses
    • Psychological health
    • Physical health
    • Health-related behaviors
  – Foundational and methodological papers

• 20-year anniversary review article
  – Published in Annals of Epidemiology (Belding et al., 2021; PMID: 34906635)
Respiratory Outcomes

• Self-reported physician-diagnosed
  – Asthma
    • Frequency and severity of asthma symptoms (new for 2019–21)
  – Chronic bronchitis
  – Emphysema

• Baseline: “Has your doctor or other health care professional ever told you that you have [condition]?”
• Follow-up: “In the last 3 years, has your doctor or other health care professional told you that you have [condition]?”

• Also assessed: persistent or recurring cough or shortness of breath
Combat Exposure

- Participants were asked if they had been personally exposed to (in the last 3 years):
  - Witnessing a person’s death due to war, disaster, or tragic event
  - Witnessing physical abuse (torture, beating, rape)
  - Dead and/or decomposing bodies
  - Maimed soldiers or civilians
  - Prisoners of war or refugees

- Note: Surveys included 13-item combat measure on 2007 survey
Combat Deployment and Incident Asthma Risk

- N = 75,770
- Incident cases ascertained through 2013
- Among deployers, no association between asthma risk and multiple deployments and deployment duration

Burn Pit Proximity and Respiratory Health

- 2010: OASD Health Affairs requested MilCo study examining whether exposure to burn pit smoke was associated with long-term respiratory outcomes.
- Defense Manpower Data Center (DMDC) identified personnel deployed within 3 and 5 miles of 3 documented burn pits in Iraq between 2003–2008:
  - Joint Base Balad, Camp Taji, Camp Speicher
  - MilCo Panels 1–2, Army or Air Force:
    - Approx. 22,300 deployed
    - Approx. 3,500 deployed within 3 miles of burn pit site
- Final report: no associations with incident asthma, chronic bronchitis or emphysema, or respiratory symptoms

Burn Pit Emissions: Serum Biomarkers

- Defense Health Program-funded study
  - Co-PI: Dr. Aarti Gautam, Integrative Systems Biology Program, WRAIR

- Longitudinal analysis of serum collected pre- and post-deployment in relation to burn pit proximity

<table>
<thead>
<tr>
<th>miRNA expression (epigenetic changes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolites of incomplete combustion byproducts</td>
</tr>
<tr>
<td>• Polycyclic aromatic hydrocarbons (PAHs)</td>
</tr>
<tr>
<td>• Polychlorinated dibenzodioxins/furans (PCDD/Fs)</td>
</tr>
</tbody>
</table>

- Examine associations between burn pit proximity, exposure biomarkers, tobacco use (self-reported, serum cotinine), and adverse respiratory outcomes
PFAS: Serum Biomarkers

- Per- and polyfluoroalkyl substances (PFAS; “forever chemicals” in aqueous firefighting foams)
  - Sponsor: JPC-5
  - Lab: Central Arkansas VA (Dr. Andrew Morris)
- Longitudinal PFAS serum measurements in 852 firefighters (exposed) and 694 construction workers (unexposed)
- Associations with cardiometabolic health outcomes (MilCo survey, MDR, VA)
PACT Act Research: Section 504

• Section 504: directs SECVA to “conduct an epidemiological study on the health trends of veterans who served in the Armed Forces after September 11, 2001.”

• Planned: Trends in prevalence of:
  – Psychological (e.g., PTSD, depression, anxiety), physical health (e.g., cardiometabolic, autoimmune, and respiratory diseases, cancer, sensory impairment), and health-related behaviors (e.g., alcohol use, tobacco, sleep) diagnoses over time
  – Neurological diagnoses (e.g., mild cognitive impairment, Parkinson’s, dementia, migraines, sleep, prodromes) in Veterans across the life course
  – Quality of life measures (e.g., somatic symptoms, pain)
  – Sub-analyses to assess changes in trends before and after military separation
PACT Act Research: Section 510

- Section 510: reports to Congress on health effects of exposure to jet fuels used by the Armed Forces

- Planned: comprehensive analysis of serum biomarkers of fuels exposures
  - Military Occupation Specialty (MOS) codes: surrogate of potential exposure or lack of exposure to jet fuels
  - Laboratory: Military and Veteran Microbiome Consortium for Research and Education (MVM CoRE); MIRECC
Future Research Directions

• Extended follow-up of health outcomes using surveys linked with MDR, VA, and mortality data
  – Focus on specific occupations (self-reported and MOS)
  – Current survey includes items on frequency and severity of asthma symptoms
  – Smoking as a potential effect modifier of deployment-related environmental exposures
  – Planned linkage to DoD/VA Individual Longitudinal Exposure Record (ILER) with declassified deployment locations and dates
  – Additional outcomes for focused research: mortality, cancer
  – Next follow-up survey scheduled for late 2023–2025
Current and Future Cancer Research

- Cancer mortality (NHRC, VA)
  - 661 cancer deaths (2001–2018)
    - DoD Medical Mortality Registry
    - National Death Index
  - Key finding: reduced risk of cancer mortality among deployed vs. nondeployed personnel
    - Healthy deployer effect

- Deployment and melanoma risk
  - 585 cases (MDR & VHA)
  - CDMRP Melanoma Team Science Award (Iowa, UTMB, NHRC, VA)

- Future plans
  - Cancer registry linkages
    - DoD and VA
    - State cancer registries (Virtual Pooled Registry)

Expected Cumulative Cancer Cases by Year, Panels 1–4

Counts exclude *in situ* cases.

Source: Case counts based on probabilities obtained from DevCan software.
Expected Cancer Cases by Year: Common Sites (Cumulative)

Source: Case counts based on probabilities obtained from DevCan software.
Conclusions

• The Cohort offers a unique opportunity to examine the long-term effects of military-related exposures and experiences on health and well-being
  – >260,000 participants
  – Survey follow-up every 3–5 years
  – Linkage with multiple enterprise databases (DoD, VA)
  – Planned linkages with ILER and cancer registries
• These current and future capabilities make the Cohort immediately responsive to PACT Act requirements
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rudolph.p.rull2.civ@health.mil

www.millenniumcohort.org
# Millennium Cohort Program Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Launch</th>
<th>Population</th>
<th>Enrollment</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Millennium Cohort</td>
<td>2001</td>
<td>Service members</td>
<td>~260,000</td>
<td>Rull</td>
</tr>
<tr>
<td>Family Cohort</td>
<td>2011</td>
<td>Spouses of Service members</td>
<td>~29,000</td>
<td>Stander</td>
</tr>
<tr>
<td>Study of Adolescent Resilience (SOAR)</td>
<td>Fall 2022</td>
<td>Adolescent children of MilCo participants</td>
<td>TBD</td>
<td>McMaster</td>
</tr>
</tbody>
</table>
## Standardized Instruments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Construct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-Form 36</td>
<td>Physical, mental, functional health</td>
</tr>
<tr>
<td>Patient Health Questionnaire</td>
<td>Depression, anxiety, panic syndromes, binge eating, alcohol-relation problems</td>
</tr>
<tr>
<td>PTSD Checklist for DSM-5 (PCL-5)</td>
<td>Posttraumatic stress disorder</td>
</tr>
<tr>
<td>Posttraumatic Growth Inventory</td>
<td>Posttraumatic growth</td>
</tr>
<tr>
<td>CAGE</td>
<td>Alcohol problems</td>
</tr>
<tr>
<td>Department of Veterans Affairs Gulf War Survey</td>
<td>Specific wartime exposures (i.e., depleted uranium, chemical or biological warfare agents)</td>
</tr>
<tr>
<td>Deployment Risk and Resilience Inventory</td>
<td>Military and unit support</td>
</tr>
<tr>
<td>Insomnia Severity Index</td>
<td>Sleep</td>
</tr>
<tr>
<td>Adverse Childhood Experiences</td>
<td>Childhood trauma</td>
</tr>
</tbody>
</table>
VHA Outpatient and Hospitalization Trends

MCP VA Outpatient Utilization Trend

- Count of Visit
- Count of SSN

MCP VA Hospitalization Trend

- Count of Admit
- Count of SSN
## 2009 MilCo Report: Postdeployment Respiratory Outcomes


<table>
<thead>
<tr>
<th>Service Branch (n)</th>
<th>Respiratory Symptoms*</th>
<th>Chronic Bronchitis or Emphysema</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Army (18,045)</td>
<td>1.73 (1.57, 1.91)</td>
<td>1.25 (0.94, 1.67)</td>
<td>1.06 (0.77, 1.44)</td>
</tr>
<tr>
<td>Air Force (12,029)</td>
<td>1.09 (0.95, 1.26)</td>
<td>0.93 (0.59, 1.47)</td>
<td>1.04 (0.68, 1.60)</td>
</tr>
<tr>
<td>Navy/Coast Guard (7,240)</td>
<td>1.06 (0.86, 1.32)</td>
<td>0.79 (0.42, 1.46)</td>
<td>0.90 (0.49, 1.65)</td>
</tr>
<tr>
<td>Marine Corps (1,679)</td>
<td>1.49 (1.06, 2.08)</td>
<td>0.94 (0.24, 3.75)</td>
<td>0.56 (0.15, 1.98)</td>
</tr>
</tbody>
</table>

2011 Survey: 13-item Combat Screener

Deployers only: In the last 3 years (Panels 1–3) or since 2001 (Panel 4), how often have you experienced the following during deployment?

- Being exposed to smoke from burning trash and/or feces

<table>
<thead>
<tr>
<th>Panel</th>
<th>N deployed</th>
<th>Never exposed</th>
<th>Exposed 1 time</th>
<th>Exposed &gt; 1 time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11,251</td>
<td>46.3%</td>
<td>3.2%</td>
<td>50.6%</td>
</tr>
<tr>
<td>2</td>
<td>4,293</td>
<td>44.2%</td>
<td>3.7%</td>
<td>52.1%</td>
</tr>
<tr>
<td>3</td>
<td>9,428</td>
<td>46.5%</td>
<td>3.3%</td>
<td>50.2%</td>
</tr>
<tr>
<td>4</td>
<td>30,424</td>
<td>42.3%</td>
<td>3.8%</td>
<td>53.9%</td>
</tr>
</tbody>
</table>
## Incident Respiratory Diagnoses Endorsed Through 2014–16 Survey

<table>
<thead>
<tr>
<th>Panel (enrollment year)</th>
<th>Sinusitis</th>
<th>Asthma</th>
<th>Chronic bronchitis</th>
<th>Emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2001)</td>
<td>13.7%</td>
<td>4.7%</td>
<td>4.4%</td>
<td>0.91%</td>
</tr>
<tr>
<td>2 (2004)</td>
<td>7.7%</td>
<td>3.4%</td>
<td>2.3%</td>
<td>0.22%</td>
</tr>
<tr>
<td>3 (2007)</td>
<td>4.7%</td>
<td>2.0%</td>
<td>1.5%</td>
<td>0.13%</td>
</tr>
<tr>
<td>4 (2011)</td>
<td>2.3%</td>
<td>1.0%</td>
<td>0.7%</td>
<td>0.08%</td>
</tr>
<tr>
<td>Total</td>
<td>7.7%</td>
<td>3.0%</td>
<td>2.5%</td>
<td>0.43%</td>
</tr>
</tbody>
</table>
Medical Encounter Data

• Military Health System Data Repository (MDR)
  – Active duty Service members and activated Reservists
  – Inpatient and outpatient ICD-9, ICD-10, CPT codes, etc.
  – All care paid for by TRICARE, both at MTFs and private facilities

• Veterans Health Administration
  – Data Use Agreement established in 2018
Mortality Data Sources

• Cause-specific deaths
  – National Death Index
    • Current and former service members
    • Source: Defense Suicide Prevention Office
  – Armed Forces Medical Examiner System
    • Active duty and activated Reserve/National Guard
    • Includes deaths occurring OCONUS
    • Source: Armed Forces Health Surveillance Board

• Vital Status
  – Social Security Administration Death Master File
  – Veterans Affairs Beneficiary Identification & Records Locator Subsystem Death File
Survey Ascertainment: Cancer

- At baseline and each follow-up wave, participants self-report diagnoses of several diseases, including cancer:
  - Baseline: lifetime diagnosis
  - Follow-up: within the last 3 years

In the last 3 years, has your doctor or other health professional told you that you have any of the following conditions?

- Cancer

If YES, in what year were you first diagnosed? [ ] No [ ] Yes

Mark here if you were hospitalized for the condition in the last 3 years [ ] Hospitalized

Please specify: [ ]
Expected Cancer Cases by Year: All Sites (Cumulative)

Source: Case counts based on probabilities obtained from DevCan software.
## Expected Cumulative Cases of Incident Invasive Cancers by Anatomical Site, Panels 1–4

<table>
<thead>
<tr>
<th>Site</th>
<th>2020</th>
<th>2025</th>
<th>2030</th>
<th>2035</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate (male)</td>
<td>994</td>
<td>1,844</td>
<td>3,132</td>
<td>4,956</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>630</td>
<td>1,043</td>
<td>1,601</td>
<td>2,286</td>
</tr>
<tr>
<td>Lung</td>
<td>585</td>
<td>1,056</td>
<td>1,764</td>
<td>2,758</td>
</tr>
<tr>
<td>Colorectal</td>
<td>525</td>
<td>898</td>
<td>1,440</td>
<td>2,181</td>
</tr>
<tr>
<td>Melanoma</td>
<td>417</td>
<td>624</td>
<td>878</td>
<td>1,182</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>314</td>
<td>487</td>
<td>712</td>
<td>997</td>
</tr>
<tr>
<td>Thyroid</td>
<td>260</td>
<td>375</td>
<td>500</td>
<td>630</td>
</tr>
<tr>
<td>Testicular (male)</td>
<td>220</td>
<td>270</td>
<td>308</td>
<td>334</td>
</tr>
<tr>
<td>Oral</td>
<td>209</td>
<td>335</td>
<td>505</td>
<td>724</td>
</tr>
<tr>
<td>Kidney</td>
<td>206</td>
<td>344</td>
<td>535</td>
<td>785</td>
</tr>
<tr>
<td>Leukemia</td>
<td>181</td>
<td>279</td>
<td>411</td>
<td>582</td>
</tr>
<tr>
<td>Bladder</td>
<td>200</td>
<td>355</td>
<td>590</td>
<td>924</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>181</td>
<td>310</td>
<td>496</td>
<td>752</td>
</tr>
<tr>
<td>Brain</td>
<td>144</td>
<td>207</td>
<td>282</td>
<td>372</td>
</tr>
<tr>
<td>Other sites</td>
<td>706</td>
<td>947</td>
<td>1,150</td>
<td>1,248</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5,771</td>
<td>9,376</td>
<td>14,305</td>
<td>20,711</td>
</tr>
</tbody>
</table>

**Source:** Case counts based on probabilities obtained from DevCan software.